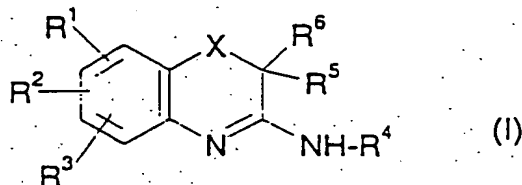


Claims

1. Compounds of Formula I, their tautomeric and isomeric forms and salts



in which

X is O, SO_m or Se,

R¹ is -(CHR⁹)_n-NR⁷-A-NR⁸-B,

R² is hydrogen or

R¹ and R² together with two adjacent carbon atoms form a 5-, 6-, 7- or 8-membered ring, which is monocyclic or bicyclic, saturated or unsaturated and in which 1 or 2 CH₂ groups can be replaced by oxygen or carbonyl, and which is substituted with (CHR⁹)_r-NR⁷-A-NR⁸-B, and can be substituted with C₁₋₄ alkyl,

R³ means hydrogen, halogen, NO₂, cyano, CF₃, -OCF₃, -S-R⁹, -O-R⁹, C₃₋₇ cycloalkyl, -NR⁹-C(=NR¹⁰)-R¹¹, -NH-CS-NR¹²R¹³, -NH-CO-NR¹²R¹³, -SO₂NR¹²R¹³, -CO-NR¹²R¹³, -CO-R¹⁴, NR¹⁵R¹⁶, C₆₋₁₀ aryl, which optionally is substituted with halogen, cyano, C₁₋₄ alkyl, -S-R⁹, or -O-R⁹,

Sub
A1

00787396-031901
TOP SECRET 9628260

5- or 6-membered heteroaryl with 1 to 4 oxygen, sulfur or nitrogen atoms,

C_{1-6} alkyl, which optionally is substituted with halogen, $-OR^9$, $-SR^9$, $-NR^{12}R^{13}$, $=NR^{12}$, $=NOC_{1-6}$ alkyl, $=N-NHaryl$, phenyl, C_{3-7} cycloalkyl or 5- or 6-membered heteroaryl,

C_{2-6} alkenyl, which optionally is substituted with halogen, $CONH_2$, $C\equiv N$ or phenyl,

C_{2-6} alkynyl, which optionally is substituted with halogen, $CONH_2$, $C\equiv N$ or phenyl,

R^4 means hydrogen or acyl,

R^5 and R^6 , independently of one another, mean hydrogen, C_{3-7} cycloalkyl, phenyl, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl radicals, which can be substituted in each case with halogen, OH, $O-C_{1-6}$ alkyl, SH, $S-C_{1-6}$ alkyl, $NR^{15}R^{16}$, 5- or 6-membered heteroaryl with 1-3 N, O or S atoms, phenyl or C_{3-7} cycloalkyl,

R^7 means hydrogen, C_{1-6} alkyl, which can be substituted with phenyl, $COOC_{1-6}$ alkyl or $CO-C_{1-6}$ alkyl,

R^8 means hydrogen, C_{1-6} alkyl, which can be substituted with phenyl, $COOC_{1-6}$ alkyl or COC_{1-6} alkyl,

A means straight-chain or branched C_{1-6} alkylene, straight-chain or branched C_{1-6} alkenylene or $-(CH_2)_p-Q-(CH_2)_q-$,

B means hydrogen or $-(CH_2)_p-U$,

Q means C_{3-7} cycloalkyl, indanyl, 5-, 6- or 7-membered saturated heterocycloalkyl with 1-2 N, O or S atoms,

Sub
A1

FILED "96278260

Sub
A1

C_6-C_{10} aryl or 5- or 6-membered heteroaryl with 1-3 N, O or S atoms, which can be anellated with benzene, U means hydrogen, C_{1-6} alkyl optionally substituted with halogen, C_{3-7} cycloalkyl, indanyl, C_{7-10} bicycloalkyl, C_{6-10} aryl or 5- or 6-membered heteroaryl with 1-3 N, O or S atoms, which can be anellated with benzene, whereby the aryl and heteroaryl radical can be substituted with halogen, C_{1-4} alkyl, C_{1-4} alkoxy, CF_3 , NO_2 , NH_2 , $N(C_{1-4} \text{ alkyl})_2$, cyano, $CONH_2$, $-O-CH_2-O-$, $-O-(CH_2)_2-O-$, SO_2NH_2 , OH, phenoxy or $COOC_{1-4}$ alkyl, or

R^8 and B together with the nitrogen atom form a 5- to 7-membered saturated heterocycle, which can contain another oxygen, nitrogen or sulfur atom and can be substituted with C_{1-4} alkyl, phenyl, benzyl or benzoyl or form an unsaturated 5-membered heterocycle, which can contain 1-3 N atoms and can be substituted with phenyl, C_{1-4} alkyl or halogen, or

R^7 and A together with the nitrogen atom form a 5- to 7-membered saturated heterocycle, which can contain another oxygen, nitrogen or sulfur atom or forms an unsaturated 5-membered heterocycle, which can contain 1-3 N atoms,

m means 0, 1 or 2,

n and r mean 0, 1 to 6,

p and q mean 0 to 6,

R^9 and R^{10} mean hydrogen or C_{1-6} alkyl.

TOP SECRET 96E28260

R¹¹ means C₁₋₆ alkyl, -NH₂, -NH-CH₃, -NH-CN, C₆₋₁₀ aryl optionally substituted with halogen, C₁₋₄ alkyl or CF₃, or 5- or 6-membered heteroaryl with 1 to 4 nitrogen, sulfur or oxygen atoms that is optionally substituted with halogen, C₁₋₄ alkyl or CF₃,

R¹² and R¹³ mean hydrogen, C₁₋₆ alkyl, phenyl optionally substituted with halogen or C₁₋₄ alkyl, benzyl optionally substituted with halogen or C₁₋₄ alkyl, or C₃₋₇ cycloalkyl,

R¹⁴ means hydrogen, hydroxy, C₁₋₆ alkoxy, phenyl, C₁₋₆ alkyl optionally substituted with CO₂H, CO₂C₁₋₆ alkyl, hydroxy, C₁₋₄ alkoxy, halogen, NR¹⁵R¹⁶, CONR¹²R¹³, or phenyl, or C₂₋₆ alkenyl optionally substituted with phenyl, cyano, CONR¹²R¹³ or CO₂C₁₋₄ alkyl,

R¹⁵ and R¹⁶ mean hydrogen, C₁₋₆ alkyl, phenyl or benzyl or

R¹⁵ and R¹⁶ together with the nitrogen atom form a saturated 5-, 6-, or 7-membered ring, which can contain another nitrogen, oxygen or sulfur atom and can be substituted with C₁₋₄ alkyl, phenyl, benzyl or benzoyl,

whereby

if X = 0, R⁶ means methyl and R², R³, R⁴ and R⁵ mean hydrogen, R¹ is not 6-((4-aminobenzyl)aminomethyl), 6-((4-dimethylaminobenzyl)aminomethyl), 6-((4-aminobenzyl)(tert-butyloxycarbonyl)aminomethyl), or 6-((4-dimethylaminobenzyl)(tert-butyloxycarbonyl)aminomethyl).

2. Compounds according to claim 1, in which R⁵ is hydrogen.

03787396-031001

Sub
Al

3. Compounds according to claims 1-2, in which R^6 is C_{1-6} alkyl.

4. Compounds according to claims 1-3, in which R^4 is hydrogen.

5. Compounds according to claims 1-4, in which X is oxygen or sulfur.

Sub A² 6. Compounds according to claims 1-5, in which R^1 and R^2 together with two adjacent carbon atoms mean a 3- to 8-membered, preferably 5- to 6-membered ring, which is substituted with $-(CHR^9)_r-NR^7-A-NR^8B$.

Sub A³ 7. Compounds according to claim 6, in which $r = 0$.

Sub A⁴ 8. Compounds according to claims 1-7, in which A means a straight-chain or branched C_{1-6} alkylene or $-(CH_2)_p-Q-(CH_2)_q-$, and p and q mean 1-4.

9. Compounds according to claim 1, in which U means hydrogen, alkyl that is optionally substituted with halogen, C_{3-7} cycloalkyl and optionally substituted phenyl.

Sub AS 10. 6-((3-Aminomethyl)-benzyl-aminomethyl)-3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6-(meta-(N-[3-keto-2-methyl-2H-1,4-benzoxazin-6-yl]-methyl-aminomethyl-benzyl-aminomethyl)-3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6-(meta-(N-[3-amino-2-methyl-2H-1,4-benzoxazin-6-yl]-methyl-aminomethyl-benzyl-aminomethyl)-3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6-((4-aminomethyl)-benzyl-aminomethyl)-3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- (para- (N- [3-amino-2-methyl-2H-1,4-benzoxazin-6-yl] -methyl-aminomethyl) -benzyl-aminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- (para- (N- [3-keto-2-methyl-2H-1,4-benzoxazin-6-yl] -methyl-aminomethyl) -benzyl-aminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((3-aminomethyl-cyclohex-1-yl) -methyl-aminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- (3- (N- [3-amino-2-methyl-2H-1,4-benzoxazin-6-yl] -methyl-aminomethyl) -cyclohex-1-ylmethyl-aminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((omega-aminobutyl-aminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((omega-aminopentyl-aminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((omega-aminohexyl-aminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((3- [4-nitrobenzyl] -aminomethyl) -benzylaminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((3- [2-methylbenzyl] -aminomethyl) -benzylaminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((3- [2,4-dichlorobenzyl] -aminomethyl) -benzylaminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((3- [3-chlorobenzyl] -aminomethyl) -benzylaminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

6- ((3- [3,4-dichlorobenzyl] -aminomethyl) -benzylaminomethyl) -3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride

Sub
AS

FOI b7E b7C b7D b7F b7G b7H b7I b7J b7K b7L b7M b7N b7O b7P b7Q b7R b7S b7T b7U b7V b7W b7X b7Y b7Z

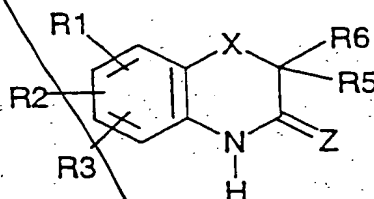
Sub AS
6-((3-benzylaminomethyl)-benzylaminomethyl)-3-amino-2-methyl-2H-1,4-benzoxazine trihydrochloride according to claim 1.

Sub A6
11. Pharmaceutical agent that contains a compound according to claims 1-10 and one or more pharmaceutically common vehicles or adjuvants.

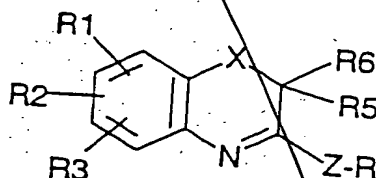
12. Use of a compound according to claims 1-10 for the production of a pharmaceutical agent for treating a disease that is triggered by NOS.

Sub A7
13. Use according to claim 11 for treatment of neurodegenerative diseases.

14. Process for the production of a compound of formula I according to claims 1-3, characterized in that a compound of formula II or its salt



IIa or

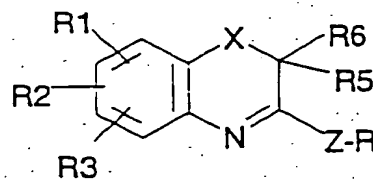
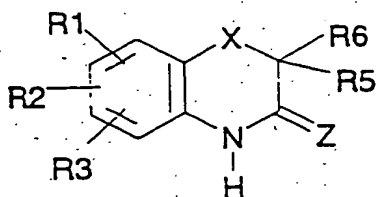


IIb

in which

Sub
A9
R¹, R², R³, R⁵, R⁶ and X have the above-mentioned meaning, Z is oxygen or sulfur and R means C₁₋₆ alkyl, is reacted with ammonia or primary amines, whereby existing amino groups are optionally intermediately protected and optionally then acylated, the isomers are separated or the salts are formed.

15. Compounds of formulas IIa and IIb



in which

R¹, R², R³, R⁵, R⁶ and X have the above meaning, X is oxygen or sulfur, and R means C₁₋₆ alkyl.

add

A10

add

B4

FOOTED" 96E28260